REMARKS

Upon entry of the Amendment, Claims 1-25 are all the claims pending in the application. Claim 25 is new. Claims 13 and 16 have been amended. Claim 13 has been amended from dependent form to independent form. Further, Claim 13 has been amended to incorporate the subject matter of Claims 2, 3, and 23. Claim 16 has been amended to delete the term "preferably." Support for new Claim 25 is found in the specification, such as on page 12, line 28. Therefore, no new matter has been added.

I. Specification

The abstract of disclosure has been objected to because of the use of the phrases "said nucleic acid" and "said assistor protein."

The abstract has been amended. The phrase "said nucleic acid" has been amended to --the nucleic acid--. The phrase "said assistor protein" has been amended to --the assistor protein--.

II. Claim Objections

Claims 13-16 have been objected to because of informalities.

Specifically, Claim 13 has been objected to as depending from a withdrawn claim. Claim 13 has been amended from dependent form to independent form. Therefore, Claim 13 does not depend from a withdrawn claim.

III. Priority

The Office Action Summary and page 4 of the Office Action indicate that no certified copy of the priority document has been filed.

A certified copy of European Application No. 02254733.5 was filed during the International Phase of the present application. Under PCT Rule 17.2(a), the designated office shall not ask the applicant to furnish a copy of the priority document. Applicants enclose a copy of PCT/IB/304, indicating that the International Bureau has received the certified copy of European Application No. 02254733.5. Acknowledgement of receipt of a certified copy of European Application No. 02254733.5 is respectfully requested.

IV. Claim Rejections - 35 U.S.C. § 112

Claims 13-16 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement.

Referring to page 4 of the Office Action, the Examiner asserts that the specification is enabling for a method of generating an immune response in a mammal by administering to the mammal a liposomal composition.

Claim 13 has been amended to read that the method generates an immune response in a mammal by administering the liposomal composition to the mammal wherein the antigenic protein and the assistor protein are derived from an infectious microorganism.

Further, with respect to Claim 16, the Examiner asserts that a practitioner in the art would not be able to predict how to practice the claimed method so as to confer immunity in any animal against infection by any infectious agent, without extensive and undue experimentation.

Applicants respectfully submit that the specification is enabling for the entire scope of Claim 16. Claim 16 presently recites a method which confers immunity against infection by an infectious virus.

Page 45 of Applicants' specification provides challenge data for mice vaccinated against the influenza virus. The challenge data provides that only 7% of the tested mice appear to be susceptible to a challenge with live virus.

A person skilled in the art would consider such challenge data to demonstrate that immunity was conferred against infection by an infectious virus. A person skilled in the art would not require complete immunity. To demonstrate immunity, a person skilled in the art would expect the data to show that the vaccine is effective in a sufficient portion of the population. The challenge data shows that a sufficient level of immunity has been achieved against infection by an infectious virus.

Medical trials should be conducted on samples with sufficient sizes for statistically significant results to be shown. The challenge data are statistically significant results. The level of significance is at the 95 % confidence level. *See*, page 45, line 19 of the specification. As a result, the composition is highly effective for generating an immune response that is capable of protecting an individual from infection with an infectious organism when administered to a subject.

Claim 13 now recites that the antigenic protein and the assistor protein are derived from an infectious microorganism.

The specification is also enabling for viruses other than influenza. The co-entrapment of the nucleic acid and antigen for one strain of influenza virus elicits an immune response observable both as raised levels of Ig and resistance to live viral challenge. The effect on antibody response is also shown for nucleic acid and antigen derived from Hepatitis B virus.

The specification also provides results that viral components other than an influenza virus, such as Hepatitis B, provide a level of immune response consistent with the levels of immune response shown for influenza. For example, the Ig levels shown for influenza in Table 3 for the invention (group 1.1) are consistent with the immune response for Hepatitis B vaccine in Example 2. In Example 3, a different influenza virus is tested and the results shown in Figure 8 for the Ig levels are consistent with those for the Sichuan virus used in Example 2. Example 4 uses a multi-valent virus, including both the Sichuan and Puerto Rico influenza virus antigen components. The Ig results shown in Figures 9a to d are, again, consistent with those of Examples 1 and 3. Different types of liposomes are utilized in Example 6 for influenza entrapment and the results shown in Example 10 are consistent with the Ig levels of the liposomes used in Example 1.

The theory as to the reason the composition is effective is provided in the specification, such as from page 5 to page 11. For example, the specification explains that the co-delivery of the DNA and its cognate protein to the same cells provides a synergistic interaction in the ensuing immune response that would not be possible if the DNA were to be acquired by one antigen presenting cell and the protein by another. A person skilled in the art can apply such a theory to other types of virus to provide for an immune response without undue experimentation. In this regard, the specification provides sufficient guidance to practice the claimed method with other types of viruses.

Claim 16 has been rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite.

Referring to pages 3-4 of the Office Action, the Examiner asserts that the phrase "immunity against infection by an infectious agent, preferably a virus" renders Claim 16 indefinite. Applicants have amended Claim 16 to read "immunity against infection by an infectious virus."

V. Claim Rejections - 35 U.S.C. § 102

Claims 13-16 have been rejected under 35 U.S.C. § 102(b), as allegedly being anticipated by U.S. Patent No. 6,166,177 to Probst et al. ("Probst").

Applicants respectfully traverse.

Probst, at column 8, line 19-22, discloses that polypeptides may be incorporated into a liposome assisted for inducing protective immunity against clamidial infection. Probst does not disclose that DNA may be incorporated into a liposome. Regarding DNA, Probst at column 8, line 27-51, discloses that DNA may be delivered to a patient for expression of the DNA sequence by bacterial or viral expression systems, or biodegradable beads. Probst does not disclose that a liposome delivery system may be used to deliver the DNA. In this regard, Probst does not describe or suggest that DNA may be associated with a liposome or that the DNA is entrapped in the intravesicular space of the liposome.

Further, Probst at column 8, lines 52-59, discloses that a "DNA vaccine" may be administered simultaneously with or sequential to a polypeptide or antigen. For example, Probst discloses that administration of DNA may be followed by administration of an antigen.

Accordingly, Probst does not describe that nucleic acid and an assistor protein are associated with a liposome. As Probst discloses that a "DNA vaccine" may be administered with

the polypeptide or antigen, Probst is referring to bacterial or viral expression systems, or biodegradable beads which Probst discloses as delivering the DNA. As such, Probst fails to describe that a liposome is used for both the DNA and the polypeptide or antigen thereof. Further, the example of sequential administration is evidence that Probst does not necessarily provide that the DNA and polypeptide are in a single composition. *See*, MPEP 2112 (IV) (2005). On the contrary, it is evidence that Probst describes that the DNA and polypeptides are formulated in separate compositions.

Additionally, Claims 13-16 have been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by WO 97/28818 to Craig *et al.* ("Craig").

Applicants respectfully traverse.

Craig at page 12, lines 10-25 provides a disclosure regarding the delivery systems of a vector or nucleic acid. Accordingly, the delivery systems disclosed therein do not relate to peptide antigens. Craig does not relate to delivery of both peptide and nucleic acid. Moreover, Craig does not relate to associating both a peptide and a nucleic acid with a liposome. Further, Craig does not relate to the formulation of nucleic acid encoding an antigen sharing the same epitope as the assistor protein.

Craig at page 24, line 30 to page 25, line 11, discloses methods of preparing cell-targeting liposomes containing nucleic acid. There is no description regarding peptide antigens. Further, there is no description regarding peptides sharing epitopes with the products encoded by the nucleic acid. Furthermore, there is no description that the nucleic acid is entrapped in the intravesicular space of these targeted liposomes.

There is also no mention of liposomal systems of any type in the section concerning pharmaceutical formulations. *See*, page 40, line 26 to page 43, line 33.

Additionally, Craig fails to describe a nucleic acid encoding an antigenic protein or portion thereof that shares at least one epitope with the assistor protein. Craig at page 4, lines 34-35 discloses that the first and second epitope may comprise an immunodominant epitope of influenza NP. Craig does not disclose that the first and second epitope may have the same immunodominant epitope. Influenza HP has several epitopes that are considered immunodominant.

Craig at page 4, lines 29-33 are epitopes of the same antigen, or epitopes of the same infectious agent or organism. There is no disclosure that the epitopes themselves are the same.

Craig discloses producing complexes at page 56, lines 12 to 19, and page 58, lines 27 to 38. The complex is made by mixing together a K6ClII peptide that contains an epitope of influenza A nucleo protein and a stretch of lysine residues for ionic interaction with the backbone of the DNA. The nucleic acid is pCMVb or pCMVluc. There is no disclosure that pCMVb encodes the same protein as the antigen of the complex. There is also no disclosure that pCMVluc encodes the same protein as the antigen of the complex. Craig discloses that pCMVluc encodes luciferase, which is not the same protein as the antigen of the complex. *See*, Figure 6.

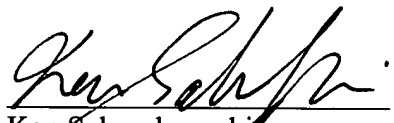
In an effort to advance prosecution and without admitting to a *prima facie* case, the claimed method also provides for unexpected results over both Probst and Craig. Example 1 provides a comparison of the results for liposomally co-entrapped nucleic acid and assistor

protein (group 1.1) with the results for other formulations in which the nucleic acid and the assistor protein are not liposomally co-entrapped (groups 1.2 to 1.12). With respect to group 1.1, the results on total Ig against the relevant antigen itself show an effect after a single dose, 16 days post administration. *See*, Table 3 of Applicants' specification. Even after 28 days from one dose, an effect is clearly apparent. In contrast, groups 1.2 to 1.12 fail to show the level of immune response provided by group 1.1. For example, groups 1.6 and 1.9 provide little immune response. Group 1.6 involved an admixture of liposomally entrapped components. Group 1.9 involved non-entrapped components.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



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PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION CONCERNING SUBMISSION OR TRANSMITTAL OF PRIORITY DOCUMENT

(PCT Administrative Instructions, Section 411)

To:

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Date of mailing (day/month/year) 18 August 2003 (18.08.03)	
Applicant's or agent's file reference HMJ03575WO	**IMPORTANT NOTIFICATION**
International application No. PCT/GB03/02935	International filing date (day/month/year) 07 July 2003 (07.07.03)
International publication date (day/month/year) Not yet published	Priority date (day/month/year) 05 July 2002 (05.07.02)
Applicant LIPOXEN TECHNOLOGIES LIMITED et al	

1. The applicant is hereby notified of the date of receipt (except where the letters "NR" appear in the right-hand column) by the International Bureau of the priority document(s) relating to the earlier application(s) indicated below. Unless otherwise indicated by an asterisk appearing next to a date of receipt, or by the letters "NR", in the right-hand column, the priority document concerned was submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b).

2. This updates and replaces any previously issued notification concerning submission or transmittal of priority documents.

3. An asterisk(*) appearing next to a date of receipt, in the right-hand column, denotes a priority document submitted or transmitted to the International Bureau but not in compliance with Rule 17.1(a) or (b). In such a case, **the attention of the applicant is directed** to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

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Priority date	Priority application No.	Country or regional Office or PCT receiving Office	Date of receipt of priority document
05 July 2002 (05.07.02)	02254733.5	EP	01 Augu 2003 (01.08.03)

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